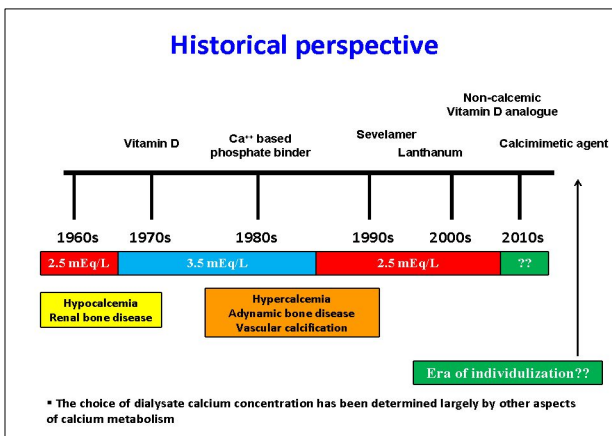
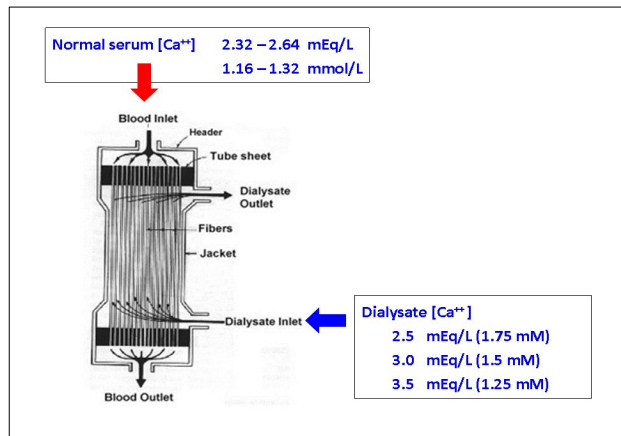
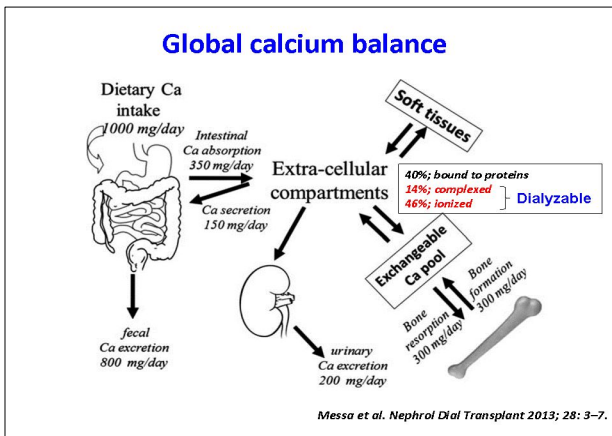


Optimal Dialysate Calcium Concentration

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CONTENTS
 K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease

9.1 The dialysate calcium concentration in hemodialysis or peritoneal dialysis **should be 2.5 mEq/L (1.25 mmol/L).** (OPINION)

9.2 Higher or lower dialysate calcium levels are indicated in selected patients. (OPINION)

KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD)

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Supplement to Kidney International

4.1.3: In patients with CKD stage 5D, we suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/l (2.5 and 3.0 mEq/l) (2D).

- The final vote on this recommendation was 16 in favor and 1 vote against.
- The KDIGO Work Group felt that, in general, a dialysate calcium concentration of 1.25 mmol/l (2.5 mEq/l) would be a near-neutral calcium balance for most patients.
- At present, it is probably wise to maintain flexibility with dialysate calcium concentrations, which should be individualized, whenever possible, to meet specific patient requirements.

Worldwide practice- results from DOPPS

The average dialysate calcium concentration was 2.9 mEq/L
Almost 60% of patients exceeding 2.5 mEq/L

Low dialysate calcium (≤ 2.5 mEq/L)	40.5 % (30717,629)
Japan	19.8 % (64/2,123)
Europe	23.9 % (101/1,839)
U.S.A	64.1 % (142/3,667)

Young EW et al. *Kidney Int* 2005; 67: 1179-1187.

Optimal dialysate calcium concentration

- Calcium mass balance
- Cardiovascular morbidity
- Hemodynamic stability on dialysis
- Mineral bone disorder

Calcium mass balance

Table. Estimated calcium balance in hemodialysis patients

Calcium balance using 3.5 mEq/l Ca⁺⁺ dialysate
Positive Ca flux : +896 mg/4 hr dialysis or +2,688 mg/wk (384 mg/d)
Dietary intake of Ca -800 mg/dl
Fractional absorption -152 mg/d (19%)
Total Ca balance +536 mg/d

Calcium balance using 2.5 mEq/l Ca⁺⁺ dialysate
Positive Ca flux : +150 mg/4 hr dialysis or +450 mg/wk (64 mg/d)
Dietary intake of Ca -800 mg/dl
Fractional absorption -152 mg/d (19%)
Total Ca balance +216 mg/d

Calcium balance using 1.5 mEq/l Ca⁺⁺ dialysate
Positive Ca flux -230 mg/4 hr dialysis or -690 mg/wk (-100 mg/d)
Dietary intake of Ca -800 mg/dl
Fractional absorption -152 mg/d (19%)
Total Ca balance +52 mg/d

Hsu et al. *Am J Kidney Dis* 1997; 29: 641-649.
Hsu et al. *Am J Kidney Dis* 1991; 18: 217-224.

Calcium mass balance during hemodialysis

	B-side			D-side		
	Diffusive	Convective	Global	Diffusive	Convective	Global
DCa 1.5 (n = 22)						
Mean ± SD	229 ± 103	-137 ± 60	93 ± 112	-404** ± 130	138 ± 60	-266** ± 116
Range	+71/-519	-14/-222	-108/+337	-212/-620	+15/+232	-76/-490
DCa 1.25 (n = 22)						
Mean ± SD	58* ± 81	-115 ± 32	-57* ± 82	-101**** ± 170	119 ± 33	18* ± 179
Range	-157/+189	-35/-186	-288/+110	-477/+135	+36/+191	-385/+236

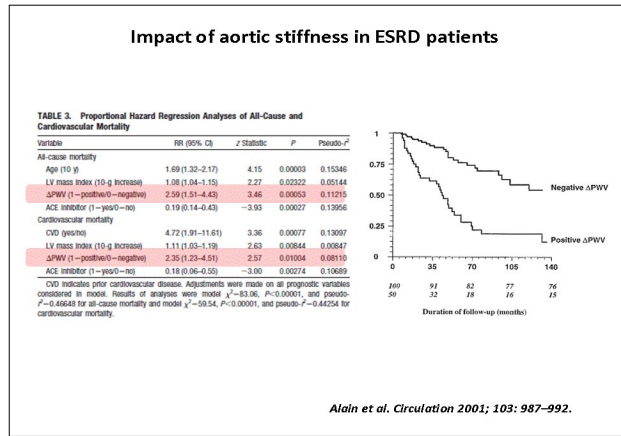
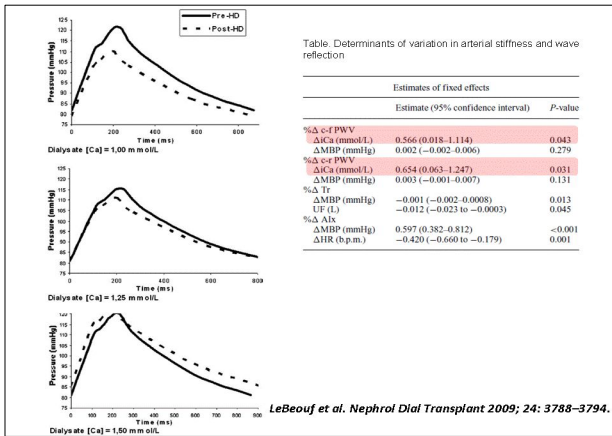
Calcium mass balance correlate ionized Ca⁺⁺ gradient between dialysate and blood ionized Ca⁺⁺

Bosticardo et al. *Nephrol Dial Transplant* 2012; 27: 2489-2496.

Cardiovascular mortality

Higher serum calcium concentration are associated with an increased risk of death

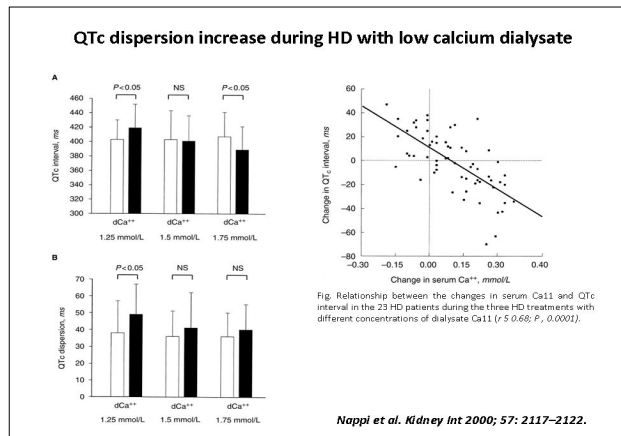
Bloch et al. *J Am Soc Nephrol* 2004; 15: 2208-2218.



Dialysate calcium concentration and overall mortality - results from DOPPS

Baseline lab measure	RR (95% CI) P value		
	All-cause mortality*	Cardiovascular mortality*	Risk of new parathyroidectomy ^b
Phosphorus (per 1mg/dL)	1.04 (1.02-1.06) 0.0003	1.09 (1.05-1.12) <0.0001	1.17 (1.09-1.25) <0.0001
Albumin-corrected calcium (per 1 mg/dL)	1.10 (1.06-1.15) <0.0001	1.14 (1.07-1.23) <0.0001	1.58 (1.35-1.85) <0.0001
Calcium-phosphorus product (per 5 mg ² /dL ²)	1.02 (1.02-1.03) 0.0001	1.05 (1.05-1.05) <0.0001	1.11 (1.10-1.12) <0.0001
PTH (per 100 pg/mL)	1.01 (1.00-1.02) 0.01	1.02 (1.00-1.03) 0.02	1.07 (1.05-1.09) 0.03
Dialysate calcium (per 1 mEq/L)	1.13 (1.03-1.25) 0.01	1.09 (0.92-1.30) 0.30	0.57 (0.35-0.95) 0.02

Young EW et al. *Kidney Int* 2005; 67: 1179-1187.



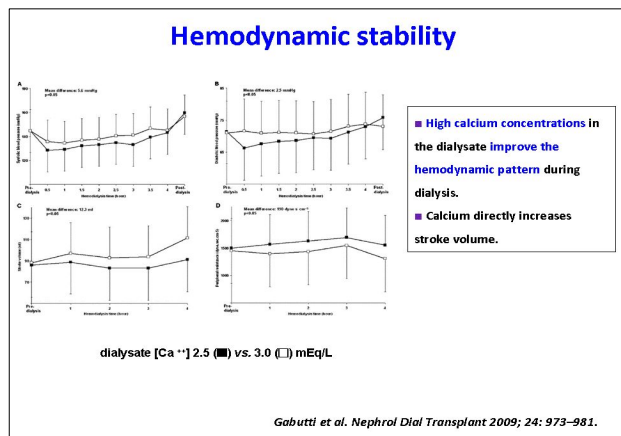
Dialysate Calcium Concentration and the Risk of Sudden Cardiac Arrest in Hemodialysis Patients

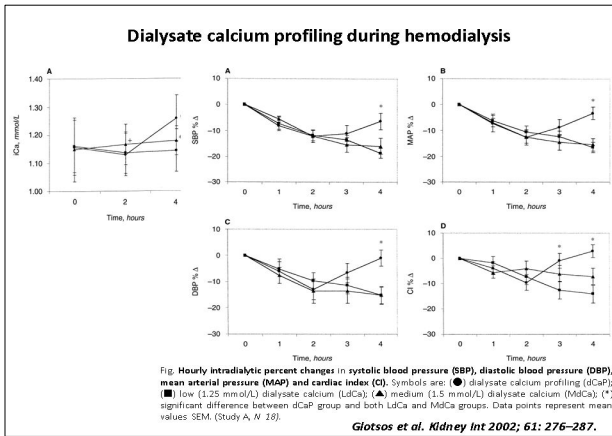
Table 2. Unadjusted and adjusted associations between relevant factors related to calcium homeostasis and risk of sudden cardiac arrest

Parameter	Unadjusted OR (95% CI)	P Value	Adjusted* OR (95% CI)	P Value
Predialysis corrected serum calcium (per 1 mg/dl increase)	1.10 (1.00-1.20)	0.05	1.10 (1.00-1.30)	0.05
Dialysate calcium=2.5 meq/L	2.00 (1.40-2.80)	<0.001	2.00 (1.40-2.80)	<0.001
Serum-to-dialysate calcium gradient (per 1 meq/L increase)	1.40 (1.10-1.60)	<0.001	1.40 (1.10-1.80)	0.002
QT medication exposure	1.20 (1.00-1.50)	0.06	1.00 (0.80-1.30)	0.80

*Adjusted for history of coronary artery disease or congestive heart failure; number of years on dialysis; prescription of calcium-containing medication, vitamin D, antiarrhythmic medication, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, and β-blockers; potassium dialysate assignment and percent fluid removed during treatment; and serum potassium, bicarbonate, creatinine, albumin, and hemoglobin values.

Pun et al. *Clin J Am Soc Nephrol* 2013; 8: 797-803.





Mineral bone disorder

Table. Effect of dialysate calcium concentration on PTH and calcium balance during HD

Parameter	ICa = 2.5 mEq/L	ICa = 2.75 mEq/L	ICa = 3.0 mEq/L	P ^a
Treatment time (min)	257.0 ± 0.8	257.2 ± 0.8	257.0 ± 0.8	0.6
Body weight pre (kg)	79.5 ± 19.8	79.9 ± 20.5	79.4 ± 20.0	0.1
Body weight post (kg)	76.4 ± 19.4	76.9 ± 20.2	76.2 ± 19.6	0.1
Volume of ultrafiltration (L)	3.1 ± 1.0	3.0 ± 0.8	3.2 ± 0.7	0.7
Plasma total protein pre (g/dL)	6.0 ± 0.8	6.1 ± 0.7	6.1 ± 0.8	0.8
Plasma total protein post (g/dL)	7.2 ± 0.7	7.2 ± 0.6	7.2 ± 0.7	0.4
Blood pH pre	7.37 ± 0.05	7.37 ± 0.04	7.37 ± 0.04	1.0
Blood pH post	7.47 ± 0.03	7.46 ± 0.03	7.47 ± 0.05	0.6
Blood bicarbonate pre (mEq/L)	20.2 ± 2.0	20.0 ± 1.6	20.3 ± 2.0	0.9
Blood bicarbonate post (mEq/L)	24.6 ± 1.3	25.3 ± 1.5	24.4 ± 1.8	0.1
Plasma water iCa pre (mEq/L)	2.48 ± 0.12	2.50 ± 0.14	2.52 ± 0.10	0.8
Plasma water iCa post (mEq/L)	2.40 ± 0.08	2.56 ^b ± 0.12	2.68 ^{b,c} ± 0.10	<0.001
iCa mass balance (mg)	-97 ± 128	+187 ^b ± 146	+326 ^{b,c} ± 253	<0.001
iCa mass balance (mg)	+75 ± 122	+182 ^b ± 125	+293 ^{b,c} ± 228	<0.001
Plasma PTH pre (pg/mL)	468 ± 418	550 ± 675	578 ± 452	0.8
Plasma PTH post (pg/mL)	692 ± 678	490 ± 514	479 ± 559	0.4
Δ Plasma PTH (post - pre) (pg/mL)	+225 ± 312	-68 ± 325 ^b	-99 ± 432 ^b	<0.02
Δ Plasma PTH (post - pre) (%)	+47 ± 30	-12 ± 9 ^b	-17 ± 15 ^b	<0.05

Basile et al. Am J Kidney Dis 2011; 59: 92-101.

Improvement of bone and mineral parameters related to adynamic bone disease by diminishing dialysate calcium

- To compare the effects of 2.5 mEq/L and 3.5 mEq/L calcium dialysate on mineral bone disorder
- 52 patients with predialysis intact PTH < 100 pg/ml

Pre HD parameter unit	LCD			HCD		
	Baseline	3 months	6 months	Baseline	3 months	6 months
iCa Pre HD	2.44±0.20	2.32±0.19 ^a	2.39±0.19	2.46±0.27	2.31±0.19 ^a	2.39±0.17 ^a
Corrected iCa Pre HD	2.53±1.02	2.39±1.01 ^a	2.50±1.02	2.51±0.36	2.37±0.21 ^a	2.54±0.26 ^a
iCa Post HD	2.41±0.19	2.34±0.17	2.48±0.20 ^b	2.65±0.18 ^c	2.50±0.17 ^{b,c}	2.63±0.19 ^{b,c}
Corrected iCa Post HD	2.50±0.24	2.40±0.16	2.59±0.23 ^b	2.73±0.21 ^c	2.56±0.20 ^{b,c}	2.73±0.20 ^{b,c}
iCa Pre HD	1.10±0.09	0.97±0.12 ^a	1.07±0.09 ^b	1.11±0.12	1.08±0.08 ^b	1.07±0.08
iCa Post HD	1.09±0.08	0.91±0.14 ^a	1.12±0.09 ^b	1.20±0.08 ^c	1.16±0.22 ^c	1.18±0.08 ^b
P	1.50±0.51	1.58±0.46	1.48±0.46	1.30±0.41	1.51±0.46 ^b	1.58±0.45 ^b
Ca×P	3.68±1.35	3.52±1.21	3.36±1.23	3.05±1.19	3.50±1.09	3.44±1.43
CaCO ₂	3.65±1.16	3.92±1.32	3.73±1.25	3.26±0.75	3.74±1.18 ^b	3.70±1.18
PTH pg/ml ^a	38.6±22.9	61.4±42.4 ^a	78.6±44.7 ^a	43.5±27.1	48.6±23.9	53.8±29.6 ^b
TAP U/L ^a	29.5±18.7	75.9±26.9 ^a	84.0±34.4 ^a	50.0±19.1	65.8±28.1	65.6±25.9
BAP U/L ^a	23.4±7.3	24.1±15.9	35.6±22.3 ^a	25.4±6.1	29.5±21.9	22.5±9.7 ^a

Abbreviations: iPTH: intact parathyroid hormone; TAP: total alkaline phosphatase; BAP: bone alkaline phosphatase. ^aReference values in subjects with normal renal function: iPTH 10-65 pg/ml; TAP 11-85 U/L; BAP (at 30 °C) 4-41 U/L.

^a Each significant alteration mentioned as such implies a significant ANOVA as well. ^bp<0.05 vs. baseline. ^cp<0.05 vs. 3 months. ^dp<0.05 vs. LCD group.

Spasovski et al. Bone 2007; 41: 698-703.

Lower dialysate calcium concentration (2.5 – 3.0 mEq/L)

Advantage

- Useful to achieve neutral calcium balance
- Reduces risk of cardiovascular morbidity
- Improve bone turnover and increase PTH

Disadvantage

- Intra-dialytic hypotension
- Increase risk of arrhythmia
- Potential for negative calcium balance and PTH stimulation

Higher dialysate calcium concentration (3.0 – 3.5 mEq/L)

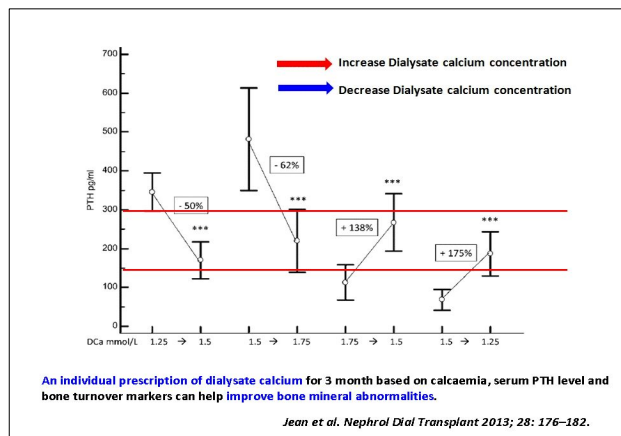
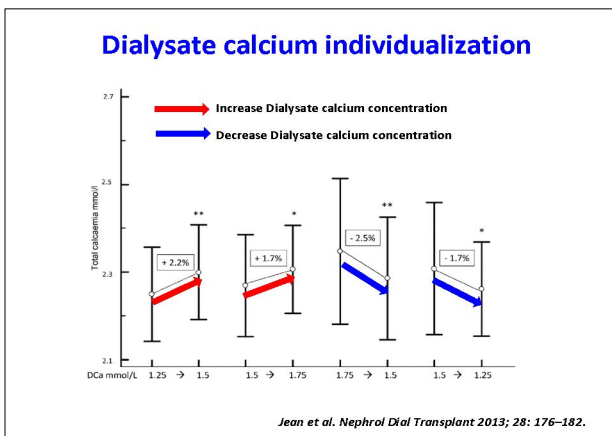
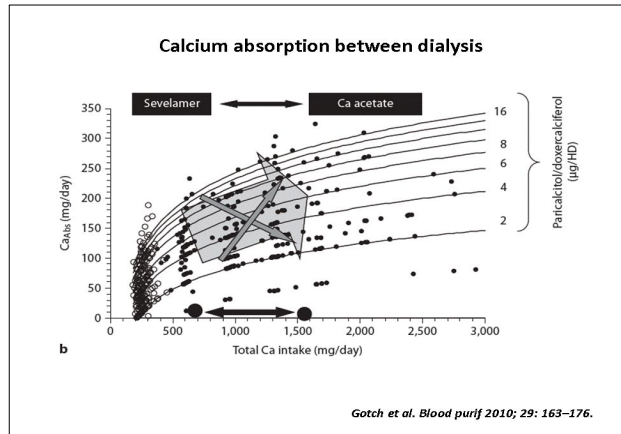
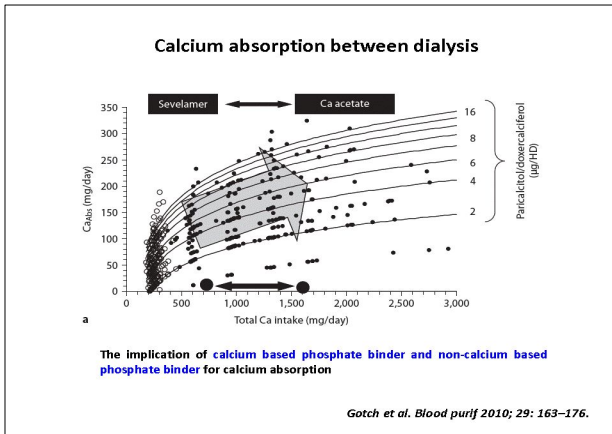
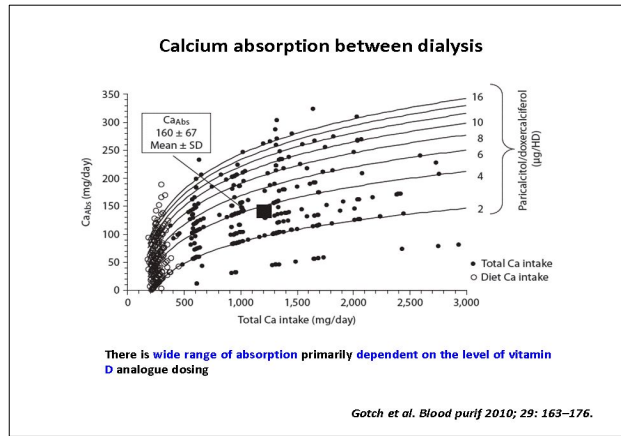
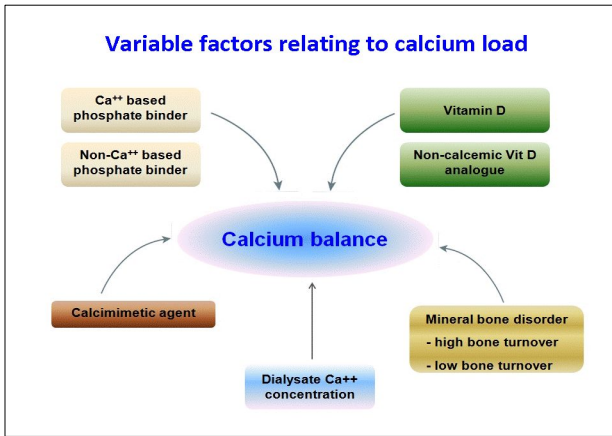
Advantage

- Improve hemodynamic stability
- Suppression of PTH

Disadvantage

- Increase risk of cardiovascular morbidity
- Limited use of vitamin D and calcium based binders
- Risk of hypercalcemia

Should dialysate calcium concentration be standardised or individualised?



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VOLUME 76 | SUPPLEMENT 113 | AUGUST 2009
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Supplement to Kidney International

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- The final vote on this recommendation was 16 in favor and 1 vote against.
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- At present, it is probably wise to maintain flexibility with dialysate calcium concentrations, which should be individualized, whenever possible, to meet specific patient requirements.

Summary

- A dialysate Ca^{++} 2.5 to 3.0 mEq/L is often the most appropriate for HD patients.
- Optimal dialysate calcium concentration
 - calcium mass balance, cardiovascular morbidity
 - mineral bone disorder, hemodynamic stability during dialysis
- Variable factors influencing calcium load
 - vitamin D vs. non-calcemic vitamin D analogue
 - calcium based phosphate binder vs. non-calcium based phosphate binder
 - calcimimetic
- Maintain flexibility with dialysate calcium concentrations, which should be individualized, to meet specific patient requirements.
 - 1) The negative dialysis Ca balance is countered by the oral administration of Ca-based phosphate binders and the use of vitamin D analogues
 - 2) The use of Ca-free phosphate binders, noncalcemic vitamin D analogues and calcimimetics allows for higher dialysate Ca baths.